General

Guideline Title

(1) Potentially curable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. (2) Potentially curable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline update.

Bibliographic Source(s)

Khorana AA, Mangu PB, Berlin J, Engebretson A, Hong TS, Maitra A, Mohile SG, Mumber M, Schulick R, Shapiro M, Urba S, Zeh HJ, Katz MHG. Potentially curable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2017 Jul 10;35(20):2324-8. [3 references] PubMed

Khorana AA, Mangu PB, Berlin J, Engebretson A, Hong TS, Maitra A, Mohile SG, Mumber M, Schulick R, Shapiro M, Urba S, Zeh HJ, Katz MHG. Potentially curable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2016 Jul 20;34(21):2541-56. [86 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

NEATS Assessment

National Guideline Clearinghouse (NGC) has assessed this guideline's adherence to standards of trustworthiness, derived from the Institute of Medicine's report Clinical Practice Guidelines We Can Trust.

= Poor = Fair = Good = Very Good = Excellent

Assessment	Standard of Trustworthiness
YES	Disclosure of Guideline Funding Source

▮▮▮▮▮	Disclosure and Management of Financial Conflict of Interests
	Guideline Development Group Composition
YES	Multidisciplinary Group
YES	Methodologist Involvement
▮▮▮▮▯	Patient and Public Perspectives
	Use of a Systematic Review of Evidence
▮▮▮▮▮	Search Strategy
▮▮▮▮▮	Study Selection
▮▮▮▮▮	Synthesis of Evidence
	Evidence Foundations for and Rating Strength of Recommendations
▮▮▮▮▮	Grading the Quality or Strength of Evidence
▮▮▮▮▮	Benefits and Harms of Recommendations
▮▮▮▮▮	Evidence Summary Supporting Recommendations
▮▮▮▮▮	Rating the Strength of Recommendations
▮▮▮▮▮	Specific and Unambiguous Articulation of Recommendations
▮▮▮▯▯	External Review
▮▮▮▮▮	Updating

Recommendations

Major Recommendations

Definitions for the rating of evidence (High, Intermediate, Low, Insufficient); types of recommendations (Evidence based, Formal consensus, Informal consensus, No recommendation); and strength of recommendations (Strong, Moderate, Weak) are provided at the end of the "Major Recommendations" field.

Clinical Question 1

After a histopathologic confirmation of pancreatic adenocarcinoma diagnosis, what initial assessment is recommended before initiating any therapy for potentially curable pancreatic cancer?

Recommendation 1.1: A multiphase computed tomography (CT) scan of the abdomen and pelvis using a pancreatic protocol or magnetic resonance imaging (MRI) should be performed for all patients with pancreatic cancer to assess the anatomic relationships of the primary tumor and to assess for the

presence of intra-abdominal metastases. Endoscopic ultrasonography and/or diagnostic laparoscopy may be used as supplemental studies and to facilitate acquisition of a biopsy specimen. A chest x-ray may be performed to stage the thorax. Other staging studies should be performed only as dictated by symptom burden. A serum level of cancer antigen (CA) 19-9 and baseline standard laboratory studies should be assayed (Type: evidence based, benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).

Recommendation 1.2: The baseline performance status, symptom burden, and comorbidity profile of a patient diagnosed with potentially curable pancreatic cancer should be evaluated carefully (Type: evidence based, benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).

Recommendation 1.3: The goals of care (including a discussion of advance directives), patient preferences, and support systems should be discussed with every patient diagnosed with potentially curable pancreatic cancer and his or her caregivers (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 1.4: Multidisciplinary collaboration to formulate treatment and care plans and disease management for patients with potentially curable pancreatic cancer should be the standard of care (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 1.5: Every person with pancreatic cancer should be offered information about clinical trials, including therapeutic trials in all lines of treatment, as well as palliative care, biorepository/biomarker, and observational studies (Type: informal consensus, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Clinical Question 2

Which patients with potentially curable pancreatic cancer should be offered a potentially curative strategy with primary tumor resection?

Recommendation 2.1: Primary surgical resection of the primary tumor and regional lymph nodes is recommended for patients with potentially curable pancreatic cancer who meet all of the following criteria: no clinical evidence for metastatic disease, a performance status and comorbidity profile appropriate for a major abdominal operation, no radiographic interface between primary tumor and mesenteric vasculature on high-definition cross-sectional imaging, and an acceptable CA 19-9 level (in absence of jaundice) suggestive of localized disease (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Clinical Question 3

Which patients with potentially curable pancreatic cancer should be offered a potentially curative strategy with preoperative therapy, followed by planned primary tumor resection?

Recommendation 3.1: Preoperative therapy is recommended for patients with pancreatic cancer who meet any of the following criteria: radiographic findings suspicious but not diagnostic for extrapancreatic disease, a performance status or comorbidity profile not currently appropriate (but potentially reversible) for a major abdominal operation, a radiographic interface between primary tumor and mesenteric vasculature on cross-sectional imaging that does not meet the criteria in Clinical Question 2, or a CA 19-9 level (in absence of jaundice) suggestive of disseminated disease (Type: evidence based, benefits outweigh harms; Evidence quality: low; Strength of recommendation: strong).

Recommendation 3.2: Preoperative therapy should be offered as an alternative treatment strategy for any patient who meets all criteria in Recommendation 2.1 (Type: evidence based, benefits outweigh harms; Evidence quality: low; Strength of recommendation: strong).

Recommendation 3.3: If preoperative therapy is administered, a complete restaging evaluation (see Clinical Question 1) is recommended after completion of treatment and before final surgical planning (Type: informal consensus, benefits outweigh harms; Evidence quality: intermediate; Strength of

recommendation: strong).

Clinical Question 4

What is the appropriate adjuvant regimen for patients with pancreatic cancer who have undergone an R0 or R1 resection of their primary tumor?

Updated Recommendation 4.1: All patients with resected pancreatic cancer who did not receive preoperative therapy should be offered 6 months of adjuvant chemotherapy in the absence of medical or surgical contraindications. The doublet regimen of gemcitabine and capecitabine is a new option; alternatively, monotherapy with gemcitabine alone or fluorouracil plus folinic acid can be offered if there are concerns about toxicity or tolerance. Adjuvant treatment should be initiated within 8 weeks of surgical resection, assuming complete recovery (Type: evidence based, benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).

Recommendation 4.2: Adjuvant chemoradiation may be offered to patients who did not receive preoperative therapy and present after resection with microscopically positive margins (R1) and/or node-positive disease after completion of 4 to 6 months of systemic adjuvant chemotherapy as outlined in Recommendation 4.1. There is clinical equipoise regarding the benefit of adjuvant radiation therapy in this setting pending results of an ongoing international randomized controlled trial (RCT) (Type: Informal consensus, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).

Recommendation 4.3: For patients with pancreatic cancer who received preoperative therapy, there are no RCT data to guide the administration of postoperative therapy. The panel recommends that a total of 6 months of adjuvant therapy (including preoperative regimen) be offered based on extrapolation from adjuvant therapy trials (Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: strong).

Clinical Question 5

When should palliative care services be initiated for patients with pancreatic cancer that is potentially curable by surgery?

Recommendation 5.1: Patients with potentially curable pancreatic cancer should have a full assessment of symptom burden, psychological status, and social supports as early as possible, preferably at the first visit. In some instances, this may indicate a need for a formal palliative care consult and services (Type: informal consensus, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Recommendation 5.2: Patients who have undergone pancreatectomy for potentially curable pancreatic cancer should receive ongoing supportive care for symptom burden that may result from the surgery and (preoperative and/or adjuvant) chemotherapy (Type: informal consensus, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Clinical Question 6

What is the recommended frequency of follow-up care or surveillance for patients with potentially curable pancreatic cancer after the administration of potentially curative multimodality therapy that includes resection?

Recommendation 6.1: In the absence of RCT evidence, the panel recommends that patients who have completed treatment of potentially curable pancreatic cancer and have no evidence of disease be monitored for recovery of treatment-related toxicities and recurrence. Visits may be offered at 3- to 6-month intervals; the role of serial cross-sectional imaging, the extent to which surveillance intervals should be prolonged over time, and the duration of recommended surveillance are all undefined (Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: moderate).

Definitions

Guide for Rating Quality of Evidence

Rating for Strength of Evidence	Definition
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (i.e., balance of benefits versus harms) and that further research is very unlikely to change either the magnitude or direction of this net effect.
Intermediate	Moderate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect; however, it might alter the magnitude of the net effect.
Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change either the magnitude and/or direction of this net effect.
Insufficient	Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. The use of the consensus opinion of experts is reasonable to inform outcomes related to the topic.

Guide for Types of Recommendations

Type of Recommendation	Definition
Evidence based	There was sufficient evidence from published studies to inform a recommendation to guide clinical practice.
Formal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. Therefore, the Expert Panel used a formal consensus process to reach this recommendation, which is considered the best current guidance for practice. The Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak"). The results of the formal consensus process are summarized in the guideline and reported in the Data Supplement (see the "Availability of Companion Documents" field).
Informal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. The recommendation is considered the best current guidance for practice, based on informal consensus of the Expert Panel. The Panel agreed that a formal consensus process was not necessary for reasons described in the literature review and discussion. The Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak").
No recommendation	There is insufficient evidence, confidence, or agreement to provide a recommendation to guide clinical practice at this time. The Panel deemed the available evidence as insufficient and concluded it was unlikely that a formal consensus process would achieve the level of agreement needed for a recommendation.

Guide for Strength of Recommendations

Rating for Strength of Recommendation	Definition
Strong	There is high confidence that the recommendation reflects best practice. This is based on (1) strong evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with no or minor exceptions; (3) minor or no concerns about study quality; and/or (4) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation.
Moderate	There is moderate confidence that the recommendation reflects best practice. This is based on (1) good evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with minor and/or few exceptions; (3) minor and/or few concerns about study quality; and/or (4) the extent of panelists' agreement. Other

Rating for Strength of Recommendation	Definition
Weak	compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.
	There is some confidence that the recommendation offers the best current guidance for practice. This is based on (1) limited evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, but with important exceptions; (3) concerns about study quality; and/or (4) the extent of panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Potentially curable pancreatic cancer

Guideline Category

Evaluation

Management

Treatment

Clinical Specialty

Gastroenterology

Geriatrics

Oncology

Radiation Oncology

Surgery

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

2016 Guideline

To provide evidence-based recommendations to oncologists and others on potentially curative therapy for patients with localized pancreatic cancer

To help with clinical decision making and specifically to address the identification of patients with pancreatic cancer who should be offered potentially curative therapy, the identification of patients who should receive preoperative and/or adjuvant treatment, the use of palliative care services both before and after treatment, and optimal oncologic surveillance

2017 Addendum

To update the Potentially Curable Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guideline by providing oncologists and other clinicians with current evidence

Target Population

Patients diagnosed with potentially curable pancreatic cancer

Interventions and Practices Considered

Evaluation

Multiphase computed tomography (CT) scan of the abdomen and pelvis
Magnetic resonance imaging (MRI)
Endoscopic ultrasonography and/or diagnostic laparoscopy as supplemental studies
Chest X-ray
Measurement of serum level of cancer antigen (CA) 19-9
Baseline standard laboratory studies
Baseline performance status, symptom burden, and comorbidity profile

Treatment/Management

Discussions of goals of care (including a discussion of advance directives), patient preferences, and support systems
Multidisciplinary collaboration to formulate treatment and care plans and disease management
Offering patients information about clinical trials, including therapeutic trials in all lines of treatment, as well as palliative care, biorepository/biomarker, and observational studies
Primary surgical resection of the primary tumor and regional lymph nodes
Preoperative therapy
Complete restaging evaluation after completion of preoperative treatment
Adjuvant chemotherapy or adjuvant chemoradiation after resection
Early full assessment of symptom burden, psychological status, and social supports
Palliative care services
Ongoing supportive care
Monitoring for recovery of treatment-related toxicities and recurrence (frequency of follow-up)

Major Outcomes Considered

- Response rate(s)
- Overall survival
- Disease-free survival
- Progression-free survival
- Adverse events

Methodology

Methods Used to Collect/Select the Evidence

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

2016 Guideline

The recommendations were developed by the multidisciplinary Expert Panel using a systematic review of articles (April 2002 to June 2015) of phase III randomized controlled trials (RCTs). Other peer-reviewed articles were used to inform the recommendations on patient and clinician communication, health disparities, and multiple chronic conditions (MCCs), as well as the section on cost implication. Articles were selected for inclusion in the systematic review of the evidence on the basis of the following criteria: included patients with potentially curable (resectable or borderline resectable) pancreatic cancer; involved phase III RCTs of preoperative (neoadjuvant) or adjuvant chemotherapy alone and/or with chemoradiotherapy and/or compared with a control arm; and written in English, with human patients.

Articles were excluded from the systematic review if they were meeting abstracts not subsequently published in peer-reviewed journals; editorials, commentaries, letters, news articles, case reports, or narrative reviews; or published in a non-English language.

Literature Search Strategy

Computerized literature searches of MEDLINE and the Cochrane Collaboration Library were performed. The searches of the English-language literature published from January 2000 to June 2015 combined pancreatic neoplasm terms and follow-up-related terms and MeSH headings. Results of the databases searches were supplemented with hand searching of the bibliographies of systematic reviews and selected seminal articles, and contributions from Expert Panel members' personal files.

Details of the literature search strategy are provided in Data Supplement 3 (see the "Availability of Companion Documents" field). A Quality of Reporting of Meta-analyses (QUOROM) Diagram that reports the results of the literature search is available in Data Supplement 4 (see the "Availability of Companion Documents" field).

2017 Addendum

Guideline Update Process

The American Society of Clinical Oncology (ASCO) uses a signals approach to facilitate guideline updating. This approach is intended to identify new, potentially practice-changing data—signals—that might translate into revised practice recommendations. The approach relies on routine literature searching and the expertise of ASCO guideline panel members to identify signals. The methodology supplement (see the "Availability of Companion Documents" field) provides additional information about the signals approach.

The recently published results of a randomized phase III study prompted an update of this guideline. The high quality of the reported evidence and the potential for its clinical impact prompted the Expert Panel to revise one of the guideline recommendations.

Number of Source Documents

2016 Guideline

There were only nine randomized controlled trials (RCTs) that met eligibility criteria and form the

evidentiary basis for some of the guideline recommendations. Twelve systematic reviews or meta-analyses of various rigor and quality were obtained, but none were deemed suitable as the basis for recommendations.

See the Quality of Reporting of Meta-analyses (QUOROM) Diagram (Data Supplement 4) in the Data Supplement (see the "Availability of Companion Documents" field) for an outline of the study selection process.

2017 Addendum

One randomized phase III study

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Guide for Rating Quality of Evidence

Rating for Strength of Evidence	Definition
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (i.e., balance of benefits versus harms) and that further research is very unlikely to change either the magnitude or direction of this net effect.
Intermediate	Moderate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect; however, it might alter the magnitude of the net effect.
Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change either the magnitude and/or direction of this net effect.
Insufficient	Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. The use of the consensus opinion of experts is reasonable to inform outcomes related to the topic.

Guide for Rating of Potential for Bias

Rating of Potential for Bias	Definitions for Rating Potential for Risk of Bias in Randomized Controlled Trials
Low risk	No major features in the study that risk biased results, and none of the limitations are thought to decrease the validity of the conclusions. The study avoids problems such as failure to apply true randomization, selection of a population unrepresentative of the target patients, high dropout rates, and no intention-to-treat analysis; and key study features are described clearly (including the population, setting, interventions, comparison groups, measurement of outcomes, and reasons for dropouts).
Intermediate	The study is susceptible to some bias, but flaws are not sufficient to invalidate the results. Enough of the items introduce some uncertainty about the validity of the conclusions. The study does not meet all the criteria required for a rating of good quality, but no flaw is likely to cause major bias. The study may be missing information, making it difficult to assess limitations and potential problems.
High risk	There are significant flaws that imply biases of various types that may invalidate the results. Several of the items introduce serious uncertainty about the validity of the conclusions. The study has serious errors in design, analysis, or reporting; large amounts of missing information; or discrepancies in reporting.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

2016 Guideline

Data Extraction

Literature search results were reviewed and deemed appropriate for full text review by two American Society of Clinical Oncology (ASCO) staff reviewers in consultation with the Expert Panel Co-Chairs. Data were extracted by two staff reviewers and subsequently checked for accuracy through an audit of the data by another ASCO staff member. Disagreements were resolved through discussion and consultation with the Co-Chairs if necessary. Evidence tables are provided in Data Supplements 1 and 2 (see the "Availability of Companion Documents" field).

Study Quality Assessment

Study design aspects related to individual study quality, strength of evidence, strength of recommendations, and risk of bias were assessed and are provided in the Data Supplement (see the "Availability of Companion Documents" field). The study quality was particularly high for this group of randomized controlled trials (RCTs). Design aspects related to the individual study quality were assessed with factors such as blinding, allocation concealment, placebo control, intention to treat, funding sources, and so on, generally indicating a low potential risk of bias for most of the identified evidence. Follow-up times varied between studies, decreasing the comparability of the results. Refer to the "Rating Scheme for the Strength of the Evidence" and Rating Scheme for the Strength of the Recommendations" fields for more extensive definitions of ratings of evidence quality, strength of recommendations, and overall potential risk of bias.

2017 Addendum

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

2016 Guideline

Panel Composition

The American Society of Clinical Oncology (ASCO) Clinical Practice Guidelines Committee (CPGC) convened an Expert Panel with multidisciplinary representation in medical oncology, radiation oncology, surgical oncology, pathology, community oncology, patient/advocacy representation, and guideline implementation. The Expert Panel was led by two Co-Chairs who had primary responsibility for the development and timely completion of the guideline.

Guideline Development Process

The Expert Panel met via webinar on several occasions and corresponded frequently through e-mail;

progress on guideline development was driven primarily by the Co-Chairs along with ASCO staff. The purpose of the meetings was for members to contribute content, provide critical review, interpret evidence, and finalize the guideline recommendations based upon the consideration of the evidence. All members of the Expert Panel participated in the preparation of the draft guideline document.

Development of Recommendations

The guideline recommendations were crafted, in part, using the GuideLines Into DEcision Support (GLIDES) methodology and accompanying BRIDGE-Wiz software™. This method helps guideline panels systematically develop clear, translatable, and implementable recommendations using natural language, based on the evidence and assessment of its quality to increase usability for end users. The process incorporates distilling the actions involved, identifying who will carry them out, to whom, under what circumstances, and clarifying if and how end users can carry out the actions consistently. This process helps the Panel focus the discussion, avoid using unnecessary and/or ambiguous language, and clearly state its intentions.

Some recommendations are based on informal consensus by the panel because there was no randomized controlled trial (RCT) evidence.

2017 Addendum

The Expert Panel used e-mail to consider the new evidence published in the October 2016 update (Appendix Table A1, online only).

Rating Scheme for the Strength of the Recommendations

Guide for Types of Recommendations

Type of Recommendation	Definition
Evidence based	There was sufficient evidence from published studies to inform a recommendation to guide clinical practice.
Formal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. Therefore, the Expert Panel used a formal consensus process to reach this recommendation, which is considered the best current guidance for practice. The Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak"). The results of the formal consensus process are summarized in the guideline and reported in the Data Supplement (see the "Availability of Companion Documents" field).
Informal consensus	The available evidence was deemed insufficient to inform a recommendation to guide clinical practice. The recommendation is considered the best current guidance for practice, based on informal consensus of the Expert Panel. The Panel agreed that a formal consensus process was not necessary for reasons described in the literature review and discussion. The Panel may choose to provide a rating for the strength of the recommendation (i.e., "strong," "moderate," or "weak").
No recommendation	There is insufficient evidence, confidence, or agreement to provide a recommendation to guide clinical practice at this time. The Panel deemed the available evidence as insufficient and concluded it was unlikely that a formal consensus process would achieve the level of agreement needed for a recommendation.

Guide for Strength of Recommendations

Rating for Strength of Recommendation	Definition
Strong	There is high confidence that the recommendation reflects best practice. This is based on (1) strong evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with no or minor exceptions; (3) minor or no concerns

Rating for Strength of Recommendation	Definition
	about study quality; and/or (4) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation.
Moderate	There is moderate confidence that the recommendation reflects best practice. This is based on (1) good evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, with minor and/or few exceptions; (3) minor and/or few concerns about study quality; and/or (4) the extent of panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.
Weak	There is some confidence that the recommendation offers the best current guidance for practice. This is based on (1) limited evidence for a true net effect (e.g., benefits exceed harms); (2) consistent results, but with important exceptions; (3) concerns about study quality; and/or (4) the extent of panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

Cost Analysis

Cost Implications

There are limited cost-effectiveness analyses regarding the various treatment modalities used in the multidisciplinary management of potentially curable pancreatic cancer. However, the available data seem to support the recommendations outlined in the guideline. A study from the United Kingdom evaluated the cost-effectiveness of diagnostic laparoscopy for assessing resectability in pancreatic and periampullary cancer and found that diagnostic laparoscopy before laparotomy in patients with potentially curable pancreatic cancer seems to be cost effective in pancreatic cancer (but not in periampullary cancer). A similar United States (U.S.) analysis found that routine diagnostic laparoscopy was the preferred strategy, allowing for cost reductions of $10,695 per quality-adjusted life-month (QALM) in patients receiving primary surgery and $4,158 per QALM in patients receiving preoperative therapy. A recent article evaluated a decision analytic model to compare neoadjuvant therapy with primary surgery in this population, estimating costs using Medicare payment (2011 U.S. dollars). Survival was reported in QALMs. The authors found that the surgery-first approach cost $46,830 and yielded survival of 8.7 QALMs, whereas the neoadjuvant chemoradiation approach cost $36,583 and yielded survival of 18.8 QALMs. Cost-effectiveness was driven primarily because the neoadjuvant approach identified patients with early metastases or poor performance status, who were spared an ineffective or prohibitively morbid operation. A similar prior analysis by the same group also found that incremental cost-effectiveness ratios were significantly lower for high-performing centers ($5,991 per QALM) than for low-performing centers ($9,144 per QALM), supporting the recommendation for multidisciplinary approach in high-volume centers. Finally, a Markov model evaluated various surveillance approaches in the postoperative setting. Not receiving scheduled surveillance was associated with a postoperative overall survival (OS) of 24.6 months and a cost of $3,837 per patient. Clinical evaluation and cancer antigen (CA) 19-9 assay every 6 months until recurrence was associated with an OS of 32.8 months and a cost of $7,496 per patient. Additional routine imaging every 6 months incrementally increased total cost by $3,465 without increasing OS. The authors concluded that increasing the frequency and intensity of postoperative surveillance of patients after curative therapy for pancreatic cancer beyond clinical evaluation and CA 19-9 testing every 6 months increases cost but confers no clinically significant survival benefit.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

2016 Guideline

Members of the Expert Panel are responsible for reviewing and approving the penultimate version of the guideline, which is then circulated for external review and submitted to *Journal of Clinical Oncology* for editorial review and consideration for publication (see online Appendix, Table A1 in the original guideline document). All American Society of Clinical Oncology (ASCO) guidelines are ultimately reviewed and approved by the Expert Panel and the ASCO Clinical Practice Guideline Committee before publication.

2017 Addendum

The revised guideline was circulated in draft form to the Expert Panel and approved. ASCO's Clinical Practice Guidelines Committee leadership reviewed and approved the final document.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Improved identification of patients with pancreatic cancer who should be offered potentially curative therapy or should receive preoperative and/or adjuvant treatment
- Adjuvant therapy improves survival and decreases recurrence compared with surgery alone, and the administration of chemotherapy in the postoperative setting is supported by randomized phase III data.
- Among patients with potentially curable pancreatic cancer, baseline performance status and a comorbidity profile should be evaluated carefully because both have implications with regard to a patient's ability to tolerate therapy. Performance status has been consistently identified as a prognostic factor for patients with pancreatic cancer. Measurement of constructs such as frailty and performance status is important, and such measurements may be used to predict chemotherapy toxicity and surgical risk. Geriatric assessment can identify underlying issues that increase the risk of adverse outcomes of older patients undergoing major abdominal surgery.

Refer to the "Literature review and analysis" and "Clinical interpretation" sections of the original guideline document for detailed discussions of the potential benefits and harms of each recommendation.

Potential Harms

- Operative mortality of patients age ≥80 years is higher than in younger patients (age 65 to 69 years), and many are transferred to extended care facilities after surgery.
- Even on clinical trials, which enroll highly selected people with potentially curable pancreatic cancer, tolerance and completion of adjuvant therapy is challenging as a result of adverse events and toxicities. In patients undergoing surgery with curative intent, a high Charlson age-comorbidity index increased the risk of death significantly (score of ≥6 increased by threefold the odds of death) within the first year after surgery. In another study of resected pancreatic adenocarcinoma that involved multivariable analysis of 326 patients, elevated blood urea nitrogen (hazard ratio [HR], 4.34; P<.001) and a Khorana score ≥3 (HR, 2.31; *P*=.039) were associated with early mortality.
- Cancer antigen (CA) 19-9 can be falsely elevated in the presence of obstructive jaundice, a common

presentation for pancreatic cancer. Therefore, levels should be repeated after resolution of hyperbilirubinemia.
- Treatment-related toxicity. A recent systematic review showed that chemoradiation plus gemcitabine was ranked the most toxic, with significantly higher hematologic toxic effects than chemoradiation plus fluorouracil (odds ratio [OR], 13.33; 95% confidence interval [CI], 1.01 to 169.36). The authors concluded that adjuvant chemotherapy with fluorouracil or gemcitabine is optimal; adjuvant chemoradiation is less effective and more toxic.

Refer to the "Literature review and analysis" and "Clinical interpretation" sections of the original guideline document for detailed discussions of the potential benefits and harms of each recommendation.

Contraindications

Contraindications

Resection of synchronous metastatic disease, even low-volume disease, is contraindicated because survival is low.

Qualifying Statements

Qualifying Statements

- The clinical practice guidelines and other guidance published herein are provided by the American Society of Clinical Oncology, Inc. (ASCO) to assist providers in clinical decision making. The information herein should not be relied upon as being complete or accurate, nor should it be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. With the rapid development of scientific knowledge, new evidence may emerge between the time information is developed and when it is published or read. The information is not continually updated and may not reflect the most recent evidence. The information addresses only the topics specifically identified therein and is not applicable to other interventions, diseases, or stages of diseases. This information does not mandate any particular course of medical care. Further, the information is not intended to substitute for the independent professional judgment of the treating provider, as the information does not account for individual variation among patients. Recommendations reflect high, moderate, or low confidence that the recommendation reflects the net effect of a given course of action. The use of words like "must," "must not," "should," and "should not" indicates that a course of action is recommended or not recommended for either most or many cases, but there is latitude for the treating physician to select other courses of action in individual patients. In all cases, the selected course of action should be considered by the treating provider in the context of treating the individual patient. Use of the information is voluntary. ASCO provides this information on an as-is basis and makes no warranty, express or implied, regarding the information. ASCO specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. ASCO assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information, or for any errors or omissions.
- Refer to the "Health Disparities," "MCCs" and "Limitation of the Research and Future Directions" sections in the original guideline document for additional qualifying information.

Implementation of the Guideline

Description of Implementation Strategy

Guideline Implementation

American Society of Clinical Oncology (ASCO) guidelines are developed for implementation across health settings. Barriers to implementation include the need to increase awareness of the guideline recommendations among front-line practitioners and survivors of cancer and caregivers and also to provide adequate services in the face of limited resources. The guideline Bottom Line Box was designed to facilitate implementation of recommendations. This guideline will be distributed widely through the ASCO Practice Guideline Implementation Network. ASCO guidelines are posted on the ASCO Web site and most often published in *Journal of Clinical Oncology* (*JCO*) and *Journal of Oncology Practice*.

For additional information on the ASCO implementation strategy, please see the ASCO Web site.

Implementation Tools

Patient Resources

Quick Reference Guides/Physician Guides

Slide Presentation

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

End of Life Care

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Khorana AA, Mangu PB, Berlin J, Engebretson A, Hong TS, Maitra A, Mohile SG, Mumber M, Schulick R, Shapiro M, Urba S, Zeh HJ, Katz MHG. Potentially curable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2017 Jul 10;35(20):2324-8. [3 references] PubMed

Khorana AA, Mangu PB, Berlin J, Engebretson A, Hong TS, Maitra A, Mohile SG, Mumber M, Schulick R, Shapiro M, Urba S, Zeh HJ, Katz MHG. Potentially curable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2016 Jul 20;34(21):2541-56. [86 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Jul 20 (addendum released 2017 Jul 10)

Guideline Developer(s)

American Society of Clinical Oncology - Medical Specialty Society

Source(s) of Funding

American Society of Clinical Oncology (ASCO)

Guideline Committee

Resectable and Borderline Resectable Pancreatic Cancer Treatment Guideline Expert Panel

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Financial Disclosures/Conflicts of Interest

Guideline and Conflicts of Interest

The Expert Panel was assembled in accordance with the American Society of Clinical Oncology's (ASCO's) Conflict of Interest Policy Implementation for Clinical Practice Guidelines ("Policy," found at http://www.asco.org/rwc). All members of the panel completed ASCO's disclosure form, which requires disclosure of financial and other interests, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria; consulting or advisory role; speakers bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Policy, the majority of the members of the panel did not disclose any relationships constituting a conflict under the Policy.

Authors' Disclosures and Potential Conflicts of Interest

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or jco.ascopubs.org/site/ifc.

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Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

2016 Guideline

Available from the Journal of Clinical Oncology Web site .

2017 Addendum

Available from the Journal of Clinical Oncology Web site .

Availability of Companion Documents

The following are available:

Potentially curable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. Methodology supplement. Alexandria (VA): American Society of Clinical Oncology; 2016. 18 p. Available from the American Society of Clinical Oncology (ASCO) Web site .

Potentially curable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. Data supplement. Alexandria (VA): American Society of Clinical Oncology; 2016. 31 p. Available from the ASCO Web site .

Potentially curable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. Slide set. Alexandria (VA): American Society of Clinical Oncology; 2016. 23 p. Available in from the ASCO Web site .

Potentially curable pancreatic cancer: American Society of Clinical Oncology clinical practice guideline. Summary of recommendations. Alexandria (VA): American Society of Clinical Oncology; 2016. 5 p. Available from the ASCO Web site .

Patient Resources

The following is available:

Pancreatic cancer - treatment options. Patient information. 2016 May 31. Available from the Cancer.Net Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on October 27, 2016. This summary was updated by ECRI Institute on July 21, 2017. The guideline developer agreed to not review the content.

This NEATS assessment was completed by ECRI Institute on August 3, 2017. The information was verified by the guideline developer on August 25 2017.

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